DEVELOPING AN ASTROCYTE SIGNALING MODEL TO INFORM AND IMPROVE STROKE TREATMENT

PUBLIC DISTRUST OF SCIENCE: SOUTH KOREA AS A CASE STUDY TO PROVIDE INSIGHT ON THE HANDLING OF COVID-19

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SOCIOTECHNICAL SYNTHESIS

With the impacts of climate change and increased incidence of cardiovascular disease threatening to overwhelm the United States's (US) healthcare system, it is important to evaluate medical treatments and the current healthcare network to prevent further overload. The technical project aims to inform future ischemic stroke treatments by analyzing signaling pathways in brain tissue, specifically astrocytes, and the therapeutic potential of mitochondrial delivery. This assessment of the potential therapy provides insight on how to target stroke, thus allowing for more effective treatments that would decrease the caseload of healthcare workers. While the technical project focuses on the clinical side of the US healthcare system, the STS project aims to provide an analysis from the political and governmental side. The STS project does so by using Actor Network Theory to compare the healthcare networks of South Korea and the United States and identifies the key gaps and differences in the networks specifically during the COVID-19 pandemic. The STS project uses these differences to highlight improves within the US healthcare network.

The technical project analyzed how signaling pathways change in stroke compared to normal physiological differences in the aim of highlighting targets for future stroke treatment through a Boolean logic model. The model also evaluated how mitochondrial delivery impacts intra and intercellular communications through the lens of a potential therapy. Together, these two conditions ultimately aim to reduce the length of stay for stroke patients in the US and thus the overwhelming of the healthcare system. The model focuses primarily on combining multiple signaling pathways to create a network with multiple inputs and outputs to represent this complex disease state. The

analysis of intercellular communication is represented by the presence of exosomes, specialized extracellular vesicles that contain damage signals and neurotrophic factors. The model was then applied for four conditions: stroke and mitochondrial delivery, just mitochondrial delivery, just stroke, and no stroke and no mitochondrial delivery.

The model predicted that astrocytes release more exosomes following stroke and mitochondrial delivery, with the highest release from the stroke and mitochondrial delivery condition followed by just mitochondrial delivery and then just stroke conditions. These conclusions were confirmed by in vitro experiments that yielded the same results. While proteomic analysis of the exosomes is still underway, these initial results are promising as they validate the accuracy and importance of the model. The initial results also provide insight to the clinical challenges of the US healthcare system, specifically the lack of targeted treatment for stroke.

The political and governmental side of the US healthcare system is fairly separated from the clinical and scientific side of the network aside from regulatory agencies like the Food and Drug Administration (FDA) and the Centers for Disease Control (CDC). While these regulatory agencies are parts of the federal government, the federal government needs to further incorporate academic scientists and clinicians in its policy making. To analyze and prove this thesis, the STS project utilized Actor Network Theory on the healthcare systems of the US and South Korea.

The analysis of the South Korean healthcare system using Actor Network Theory highlights the gaps between the governing agencies like the Presidential cabinet and academic scientists and clinicians in the US. The recent appointment of Eric Lander to the Presidential cabinet is a step in the right direction, but the incorporation of National

Institutes of Health and CDC leaders would more closely emulate the successful network of South Korea. Additionally, this evaluation also elucidates the need for a centralized and public health insurance system within the United States to remove the burden from clinicians and patients of changing treatment due to insurance issues. South Korea's incorporation of community values such as communalism and interdependence allowed for the country's success in the pandemic, and this gap in the US network contributed to failures in handling the pandemic in the United States.

Because the US healthcare network is so complex and overwhelmed, it is important to analyze both the clinical side and the political/governmental side. Clinicians and scientists not only need better understanding of targets for treatments in cardiovascular diseases, they also need to be incorporated into policymaking at a much greater scale. Together, these projects aim to analyze both sides of this issue and work together to address the gaps in the US healthcare network.